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Evaluating intraocular lens power formula constant robustness using bootstrap algorithms

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Abstract

Background: Bootstrapping is a modern technique mostly used in statistics to evaluate the robustness of model parameters. The purpose of this study was to develop a method for evaluation of formula constant uncertainties and the effect on the prediction error (PE) in intraocular lens power calculation with theoretical-optical formulae using bootstrap techniques.

Methods: In a dataset with $N = 888$ clinical cases treated with the monofocal aspherical intraocular lens (Vivinex, Hoya) constants for the Haigis, the Castrop and the SRKT formula were optimised for the sum of squared PE using nonlinear iterative optimisation (interior point method), and the formula predicted spherical equivalent refraction (predSEQ) and the PE were derived. The PE was bootstrapped NB = 1000 times and added to predSEQ, and formula constants were derived for each bootstrap. The robustness of the constants was calculated from the NB bootstrapped models, and the predSEQ was back-calculated from the NB formula constants.

Results: With bootstrapping, the 90% confidence intervals for the a0/a1/a2 constants of the Haigis formula were −0.8317 to −0.5301/0.3203 to 0.3617/0.1954 to 0.2100, for the C/H/R constants of the Castrop formula they were 0.3113 to 0.3272/0.1237 to 0.2149/0.0980 to 0.1621, and for the A constant of the SRKT formula they were 119.2320 to 119.3028. The back-calculated PE from the NB bootstrapped formula constants standard deviation for the mean/median/mean absolute/root mean squared PE were 5.677/5.735/0.401/0.318 e-3 dpt for the Haigis formula, 5.677/5.735/0.401/0.31829 e-3 dpt for the Castrop formula and 14.748/14.790/0.561/0.370 e-3 dpt for the SRKT formula.

Conclusion: We have been able to prove with bootstrapping that nonlinear iterative formula constant optimisation techniques for the Haigis, the Castrop and the SRKT formulae yield consistent results with low uncertainties of the formula constants and low variations in the back-calculated mean, median, mean absolute and root mean squared formula prediction error.

KEYWORDS
bootstrap techniques, constant optimisation, formula prediction error, lens formula evaluation, lens power calculation, performance metrics

1 | INTRODUCTION

Lens power calculation formulae are widely used for determination of the lens power to achieve proper refractive results after cataract surgery (Savini et al., 2020; Shammas, 2004). In recent decades, modern optical biometers with a high accuracy in combination with advanced lens power calculation concepts have been developed to meet the goal of reaching the intended refraction after cataract surgery (Wendelstein et al., 2022). Today, in selected study populations, up to 50%/80% of cases result in a refraction within benchmarks of ±0.25/±0.50 dpt in formula prediction error (Savini et al., 2020).

There are several techniques for optimising formula constants: In the simple case of a single constant, the calculation concept can be reformulated to obtain an individual constant matching the biometric measures, the power of the implanted lens and the postoperative refraction (Schröder et al., 2016). In these situations, the variation in formula constants can be evaluated directly using statistical methods. However, we have to be aware that any statistical metrics such as the mean or median of these individual formula constants may not necessarily give the best solution for the refractive outcome in the entire population (Schröder et al., 2016). With formulae requiring more than one formula constant to predict the lens power such as the Haigis (Haigis et al., 2000) or Castrop formula (Langenbucher et al., 2022; Langenbucher, Szentmáry, Cayless, Weisensee, et al., 2021b; Wendelstein et al., 2022), such simple formula inversion methods cannot be used and we have to search for either linear optimisation strategies (e.g. multiple linear regression) or nonlinear iterative techniques to find the best set of formula constants (Langenbucher, Szentmáry, Cayless, Müller, et al., 2021a; Zhang et al., 2019).

Furthermore, neither technique (linear or nonlinear) offers a straight-forward way of estimating the robustness of the set of formula constants. The uncertainties of formula constants extracted in the simple case of single formula constants, for example by calculating the standard error, cannot be derived where the entire dataset has been used to extract the optimum set of formula constants (Langenbucher et al., 2022; Langenbucher, Szentmáry, Cayless, Müller, et al., 2021a; Schröder et al., 2016).

To overcome this problem, a bootstrap algorithm could be implemented. The idea behind bootstrapping is mostly based on taking a sample of N data from an entire dataset of N cases *with replacement* with many repetitions (Davison & Hinkley, 1997; Efron, 1982; Efron & Tibshirani, 1993). This means that in each sample the number of data points is equivalent to the entire dataset, but some entries are out-of-bag (Martínez-Muñoz & Suarez, 2010) whereas others are in-the-bag twice or more. This sampling strategy should mimic multiple repetitions of the 'experiment' and is fully data driven (Efron, 1982; Iskander et al., 2004). In this context, data driven means that, for example if the sample data are used for modelling, then the prediction errors of the models derived from the samples should on average match the distribution of the prediction errors of the model derived from the original dataset (Davison & Hinkley, 1997; DiCiccio & Efron, 1996; Efron, 1982; Worth & Cronin, 2001).

Bootstrap algorithms are widely used in statistics and in research disciplines where repetitions of experiments to derive the robustness of prediction models are cost or time intensive and distributions of parameters or the model prediction errors are not known (Efron, 1982; Efron & Tibshirani, 1993; Iskander et al., 2004).

The *purpose of this paper* is:

- to present a method for evaluating the robustness of sets of formula constants used to determine the appropriate intraocular lens power (using as examples the Haigis and the Castrop formula based on 3 formula constants and the SRK/T formula based on 1 formula constant for reference),
- to apply this method to a large dataset of cataract patients with preoperative biometric measures, together with data on the power of the implanted lens, and the postoperative refraction and
- to estimate the (nonparametric) confidence intervals for the formula constant triplets.

2 | MATERIALS AND METHODS

2.1 | Dataset for formula constant optimisation

In this retrospective study we analysed a dataset containing measurements from 888 eyes from a cataract population from Augen- und Laserklinik Castrop-Rauxel, Castrop-Rauxel, Germany, which was transferred to us (490 right eyes and 398 left eyes; 495 female and 392 male). The mean age was 71.2 ± 9.1 years (median: 71 years, range: 47 to 91 years). The local ethics committee (Ärztekammer des Saarlandes) provided a waiver for this study (157/21). The data were transferred to us in an anonymised fashion, which precludes back-tracing of the patient. The anonymised data contained preoperative biometric data derived with the IOLMaster 700 (Carl-Zeiss-Meditec, Jena, Germany) including: axial length AL, anterior chamber depth ACD measured from the corneal front apex to the lens front apex, lens thickness LT and the corneal front surface radius measured in the flat (R1) and in the steep meridian (R2). In all cases a 1 piece hydrophobic aspherical (aberration correcting) monofocal intraocular lens (Vivinex XC1 or XY1, Hoya Surgical Optics, Singapore) was inserted. In addition to the refractive power of the inserted lens (PIOL), the postoperative refraction (spherical equivalent SEQ = sphere +0.5·cylinder) 5 to 12 weeks after cataract surgery was measured by an experienced optometrist with trial glasses in a trial frame and recorded in the dataset. The dataset included only data with a postoperative Snellen decimal visual acuity of 0.8 (20/25 Snellen lines) or higher in order to ensure that the postoperative refraction was reliable. The relevant descriptive data on biometry, PIOL and postoperative refraction are summarised in Table 1. The Excel data (.xlsx-format) was imported into MATLAB to Matlab (Matlab 2019b, MathWorks, Natick, USA) for further processing.

TABLE 1 Explorative data from preoperative biometry (axial length AL, anterior chamber depth ACD, lens thickness LT, average corneal radius of curvature Rmean, average corneal power Kmean derived from corneal curvature using Javal keratometer index $n_K = 1.3375$), power of the implanted lens (PIOL) and postoperative refraction (spherical equivalent SEQ) with mean, standard deviation (SD), median and the lower (quantile 5%) and upper (quantile 95%) boundary of the 90% confidence interval.

N = 888	AL in mm	ACD in mm	LT in mm	Rmean in mm	Kmean in dpt	PIOL in dpt	SEQ in dpt
Mean	24.10	3.19	4.62	7.76	43.52	20.62	−0.56
SD	1.41	0.41	0.46	0.27	1.50	3.73	0.92
Median	23.90	3.18	4.59	7.77	43.48	21.0	−0.25
Quantile 5%	22.10	2.51	3.86	7.31	41.02	13.5	−2.38
Quantile 95%	26.78	3.83	5.36	8.23	46.16	26.0	0.38

2.2 | Preprocessing of the data

Custom software was written in Matlab. The patient age was derived from the date of cataract surgery and date of birth. The mean corneal radius of curvature Rmean was calculated as Rmean = ½(R1 + R2), and the mean corneal power Kmean was derived from R1 and R2 as Kmean = ½((n_K − 1)/R1 + (n_K − 1)/R2) with a keratometer index n_K, as indicated in the formula definition. Three lens power calculation concepts were considered in this paper: the Haigis formula (Haigis et al., 2000) considers the AL, ACD, and Rmean together with a formula constant triplet a0/a1/a2, the Castrop formula (Langenbucher, Szentmáry, Cayless, Weisensee, et al., 2021b, Wendelstein et al., 2022) considers AL, CCT, ACD, LT and corneal curvature of the front and back surface together with a formula constant triplet C/H/R. For simplicity and without loss of generality, the corneal thickness was set to 0.55 mm and the corneal back surface curvature Rb was derived from the corneal front surface curvature with a preset ratio of front to back surface curvature (Rb = 0.84·Rmean). For reference, we also included the SRKT formula (Retzlaff et al., 1990; Sanders et al., 1990) in this study which considers AL and Kmean (derived with a $n_K = 1.3375$) and Aconst as a single formula constant. All formulae included in this analysis were reorganised and solved for the SEQ as a function of preoperative biometrical data and PIOL. The difference between the achieved SEQ (from the postoperative follow-up examination) and the SEQ predicted by the formula was considered as the formula prediction error PE.

Formula constants (triplet a0/a1/a2, triplet C/H/R, and A constant for the Haigis, Castrop and SRKT formula) were optimised using a nonlinear iterative optimisation strategy (Trust Region Algorithm) by minimising the root mean-squared (RMS) PE of the entire dataset (Byrd et al., 1999, 2000; Langenbucher et al., 2022; Waltz et al., 2006). Formula constant optimisation was implemented using interior point methods, which refer to a family of optimisation techniques for solving linear and nonlinear convex optimisation problems (Boyd & Vandenberghe, 2004; Coleman & Li, 1994; Dikin, 1967; Karmarkar, 1984). The SEQ prediction was back-calculated using the optimised constants for each formula, and the prediction error PE was derived (Langenbucher et al., 2022; Langenbucher, Szentmáry, Cayless, Müller, et al., 2021a).

2.3 | Bootstrapping implementation

The following section outlines the strategy of bootstrapping for evaluation of the model reliability in terms of formula constant uncertainties:

1. The model prediction error PE of the *N* = 888 cases derived with the optimised formula constants was sampled NB times (NB refers to the number of bootstrap sequences) with replacement.
2. The NB bootstrapped PE was added to the SEQ prediction back-calculated using the optimised constants.
3. For each bootstrap a new set of formula constants was optimised using nonlinear iterative optimisation techniques as described before.
4. From the NB sets of formula constants the mean, median, SD and 90% confidence intervals were derived. The 90% confidence interval for the NB sets of formula constants was quoted as the 'uncertainty' of the constant (triplets).
5. For each of the NB bootstraps the model prediction error was calculated as the difference between the achieved SEQ and the formula predicted SEQ, using the individual set of formula constants.
6. The NB sequences of bootstrapped formula prediction errors as derived with (5) were used to check for trend errors of the Haigis, Castrop and SRKT formulae for axial length (long and short eyes) and Rmean (flat or steep corneal curvatures).

2.4 | Statistical evaluation

Explorative data are shown with mean, standard deviation (SD), median and 90% confidence intervals (5% quantile as the lower bound and 95% quantile as the upper bound). For evaluation of the formula trend errors, a least squares linear regression line was fitted to the bootstrapped formula prediction errors by minimising the root mean squared model error. A probability density function (PDF) plot was chosen to show the variation of the formula constants in the bootstrapped dataset.

3 | RESULTS

After optimisation of the formula constants from the entire dataset, the formula constant triplet a0/a1/a2

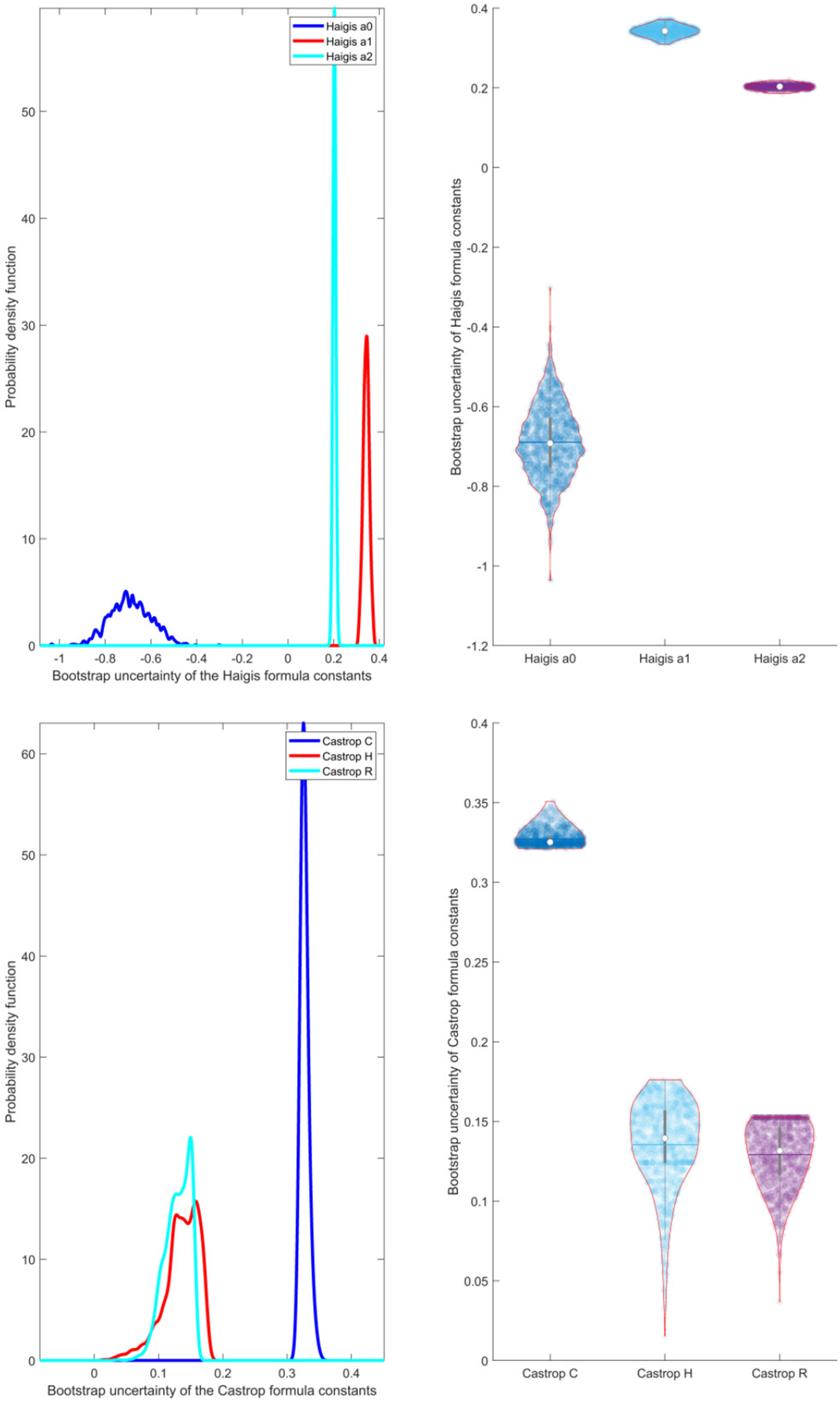

FIGURE 1 Graphs in the upper row show the PDF kernel distributions (left graph) and the respective violin plot (right graph) of the 3 formula constants a0/a1/a2 for the Haigis formula. It is obvious that the variation of a0 is much larger compared to the variation in a1 and the variation in a2. The respective 90% confidence intervals for a0/a1/a2 are calculated to be: −0.8317 to −0.5301/0.3203 to 0.3617/0.1954 to 0.2100. The graphs in the middle row display the PDF kernel distributions (left graph) and the respective violin plot (right graph) of the 3 formula constants C/H/R for the Castrop formula. From the plot we directly see that the variation of H is slightly larger than the variation in R, which is again much larger than the variation in C. The respective 90% confidence intervals for C/H/R are calculated to be: 0.3113 to −0.3272/0.1237 to 0.2149/0.0980 to 0.1621. The graphs in the lower row show the PDF kernel distribution (left graph) and the respective violin plot (right graph) of the Aconst for the SRKT formula as reference. The respective 90% confidence interval for Aconst is calculated to be 119.2320 to 119.3028.

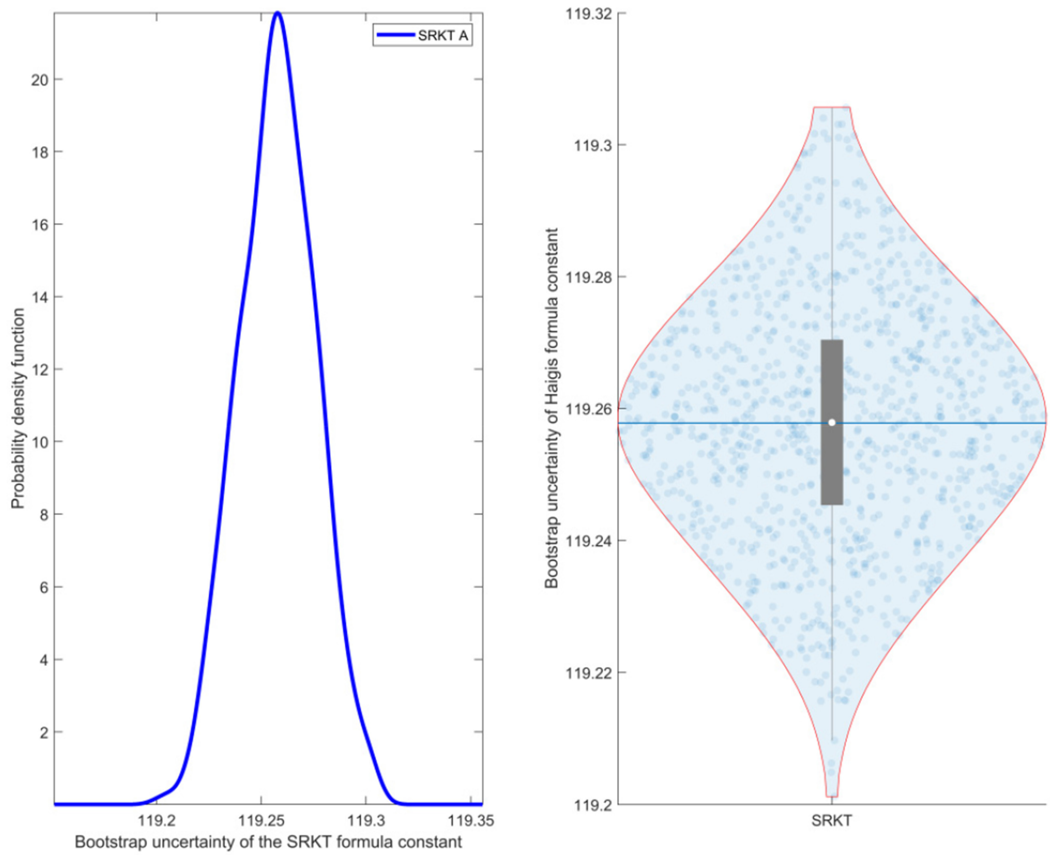

FIGURE 1 (Continued)

for the Haigis formula was −0.6852/0.3418/0.2029 and the respective mean/median/RMS prediction error PE were 0.0065/−0.0056/0.3710 dpt, respectively. For the Castrop formula, the formula constant triplet C/H/R was 0.3232/0.1523/0.1296 and the respective mean/median/RMS prediction error PE were 0.0034/0.0023/0.3451 dpt. As reference, for the SRKT formula, the Aconst was 119.2626 and the respective mean/median/RMS prediction error PE were −0.0045/−0.0134/0.4412 dpt, respectively.

A total of NB = 1000 bootstrap samples were taken from the formula prediction error with replacement. The graphs in the upper row of Figure 1 display the PDF kernel distributions (left graph) and the respective violin plot (right graph) of the 3 formula constants a0/a1/a2 for the Haigis formula. It is obvious that the variation of a0 is much larger than the variation in a1 and the variation in a2. The respective 90% confidence interval for a0/a1/a2 is calculated to −0.8317 to −0.5301/0.3203 to 0.3617/0.1954 to 0.2100. The graphs in the middle row of Figure 1 display the PDF kernel distributions (left graph) and the respective violin plot (right graph) of the 3 formula constants C/H/R for the Castrop formula. It can be seen from the plot that the variation of H is slightly larger than the variation in R, which is again much larger than the variation in C. The respective 90% confidence intervals for C/H/R are calculated as: 0.3113 to −0.3272/0.1237 to 0.2149/0.0980 to 0.1621. For reference, the graphs in the lower row of Figure 1 show the PDF kernel distribution (left graph) and the respective violin plot (right graph) of the Aconst for the SRKT formula. The respective 90% confidence interval for Aconst is calculated to be 119.2320 to 119.3028.

In a next step, these NB = 1000 sets of bootstrap formula constants were used to back-calculate the prediction error of the entire dataset (N = 888) to obtain insight into the variation of the mean and median PE. Figure 2 displays the mean PE, the median PE, the mean absolute PE and the root mean squared PE for the case where the NB = 1000 bootstrap formula constants (SRKT formula) or formula constant triplets (Haigis and Castrop formula) are tested. In the upper graph/middle graph/lower graph the situation is shown for the Haigis/Castrop/SRKT formulae, respectively. We directly see from the graphs that the SD of the mean/median/mean absolute/root mean squared formula PE is 6.23/6.49/0.37/0.13 e-3 dpt for the Haigis formula, 5.68/5.73/0.40/0.32 e-3 dpt for the Castrop formula and 14.75/14.79/0.56/0.37 e-3 dpt for the SRKT formula. For all 3 formulae under test, the variation of the mean and median PE is much larger compared to the variation of the mean absolute and root mean square PE, as a result of the formula constant optimisation strategy that was used to derive the formula constants (minimising the sum of squared PE).

In a final step, we used the back-calculated PE data from our NB = 1000 bootstraps to derive the trend error of the 3 formulae under test. Figure 3 shows the N·NB = 888 000 data points together with the linear regression analysis indicating the trend error as functions of: axial length (left graph), corneal front surface radius (middle graph) and power of the implanted intraocular lens (right graph) for the Haigis formula (upper row), the Castrop formula (middle row) and the SRKT formula

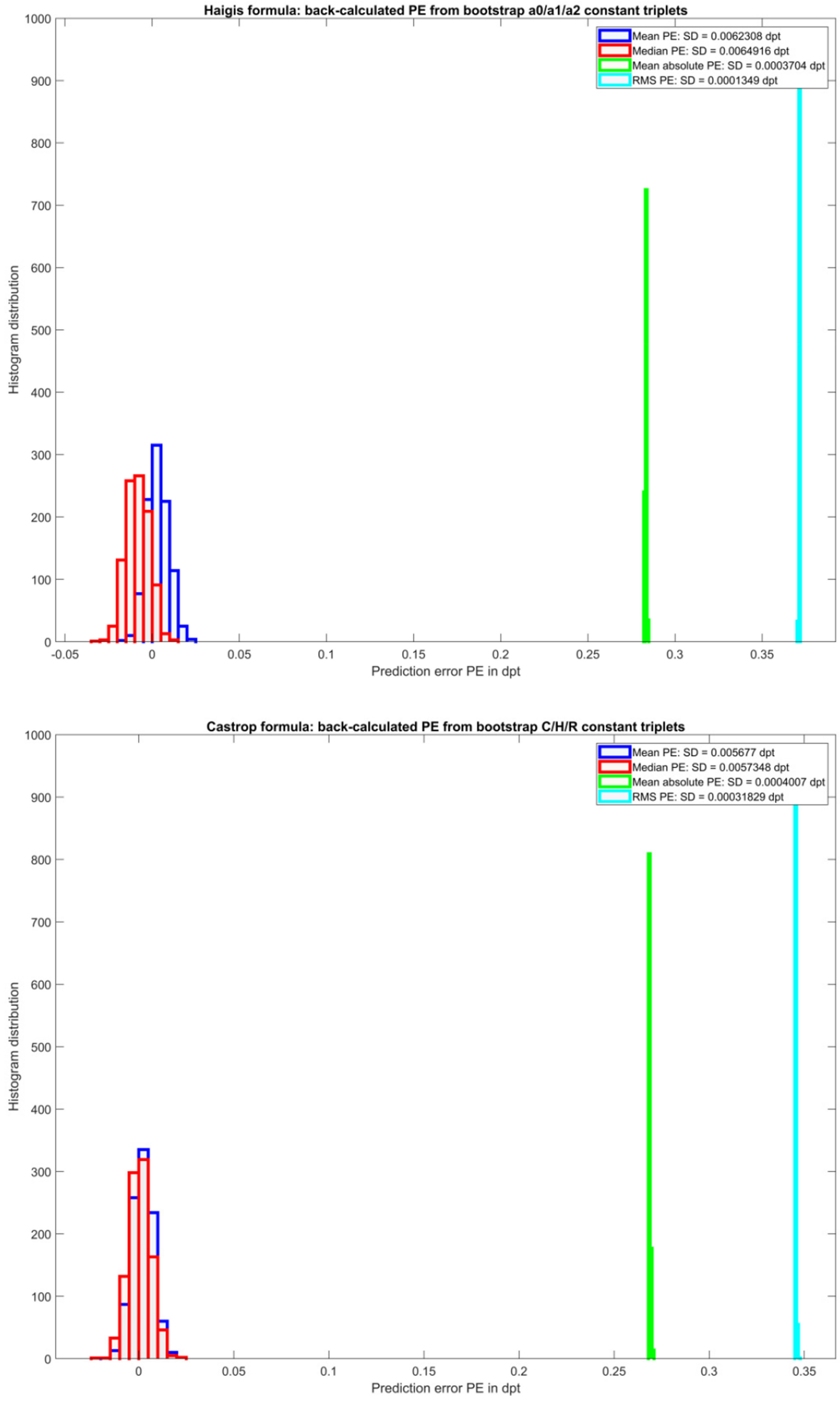

FIGURE 2 Histogram plot for the mean PE (blue), the median PE (red), the mean absolute PE (green) and the root mean squared PE (cyan) if the NB = 1000 bootstrap formula constants (SRKT formula) or formula constant triplets (Haigis and Castrop formula) are used to back-calculated the formula prediction error. The upper/middle/lower graphs show the situation for the Haigis/Castrop/SRKT formulae, respectively. The SD of the mean and median PE is much larger compared to the SD of the mean absolute and root mean squared PE for all 3 formulae (SD values provided in the figure legends). With the Haigis and the Castrop formula there is no systematic shift between the mean and median PE, whereas with the SRKT formula we can directly see from the graph that the distribution of the median PE is shifted towards positive values of PE.

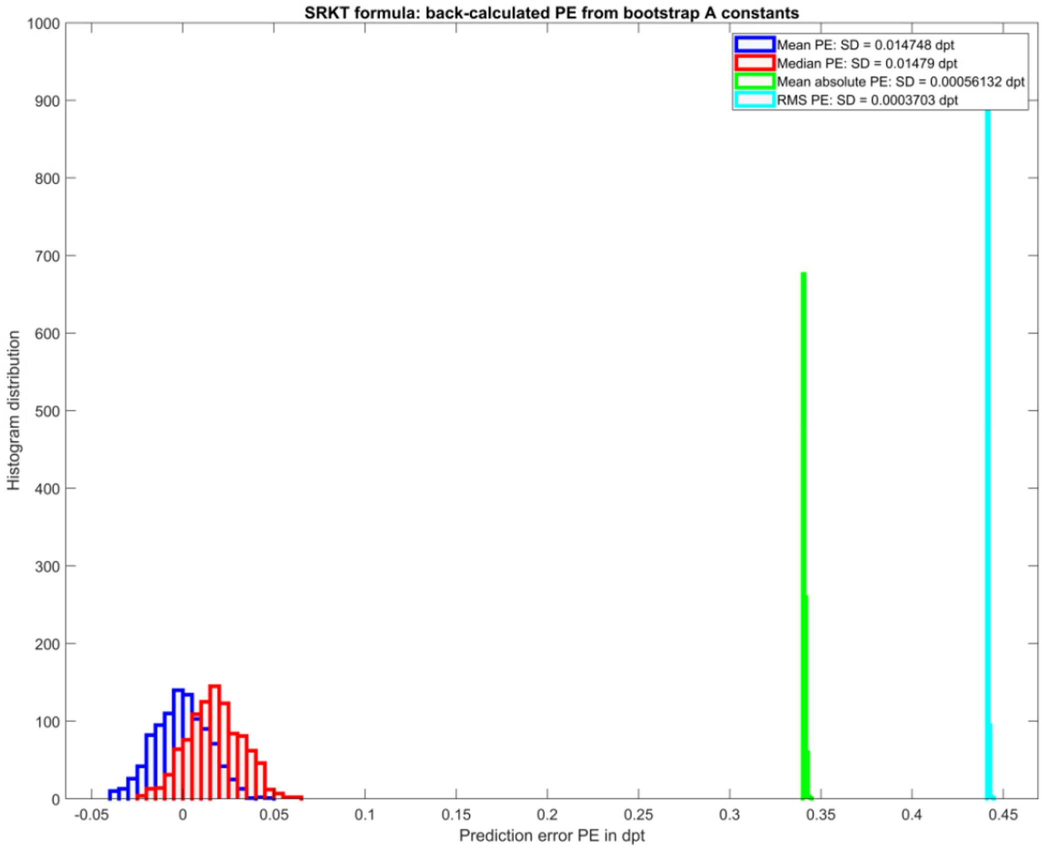

FIGURE 2 (Continued)

(lower row). The Haigis formula shows a slightly positive (intercept −0.2438; slope: 0.0102)/moderate negative (intercept 2.2509; slope: −0.2894)/slightly negative trend error (intercept 0.2365; slope: −0.0113) for AL/Rmean/IOLP. In contrast, the Castrop formula shows a slightly positive (intercept −0.2057; slope: 0.0086)/slightly negative (intercept 0.6640; slope: −0.0852)/no noticeable trend error (intercept 0.0611; slope: −0.0029) for AL/Rmean/IOLP. For reference, the SRKT formula shows a moderate positive (intercept −1.2345; slope: 0.0512)/strong positive (intercept −5.7724; slope: 0.7432)/slightly positive trend error (intercept −0.1542; slope: 0.0074) for AL/Rmean/IOLP.

4 | DISCUSSION

Bootstrapping is a commonly used technique in statistics for evaluating the robustness or reliability of model parameters where repetitions of the experiment would be too costly or time-consuming (Davison & Hinkley, 1997; Efron, 1982; Efron & Tibshirani, 1993). However, bootstrapping has not yet been extensively applied in applications in ophthalmology (Iskander et al., 2004). In cataract surgery, bootstrapping techniques are not required for lens power calculation formulae dealing with a single formula constant, as re-formulating the lens power formulae and solving for the individual formula constant for each clinical case is sufficient and gives us some insight to the distribution of the formula constant in a dataset (Aristodemou et al., 2011; Langenbucher, Szentmáry, Cayless, Müller, et al., 2021a; Schröder et al., 2016). However, where formulae having more than one formula constant are involved, the entire dataset has to be used, for example to derive the set of formula constants and there is, therefore, no information about the variation of each formula constant within the set (Schröder et al., 2016). In these cases with more than 1 formula constant, bootstrapping can be used to have a common and straight-forward concept for deriving the robustness of formula constants.

When dealing with a very large dataset, it would be possible to split the data randomly into multiple subsets and to fit models to each subset. However, in a real life scenario, the number of data points is limited, and bootstrapping the data with sampling and replacement offers a powerful option to simulate multiple repetitions of the experiment. One of the major benefits of bootstrapping is that this technique is fully data driven (DiCiccio & Efron, 1996; Efron & Tibshirani, 1993; Worth & Cronin, 2001). This means that by sampling the original dataset with replacement, on average the distributions of the input parameters and the target parameters remain unchanged. In addition, evaluating the uncertainty of model parameters using bootstrap techniques and confidence intervals eliminates the need to estimate the characteristic parameters of the distributions such as mean or standard deviations (Davison & Hinkley, 1997; Iskander et al., 2004).

In the present study, we used a dataset with $N = 888$ data points and optimised the a0/a1/a2 constant triplet for the Haigis formula, the C/H/R constant triplet for the Castrop formula, and for reference, the A constant for the SRKT formula in terms of minimising the sum

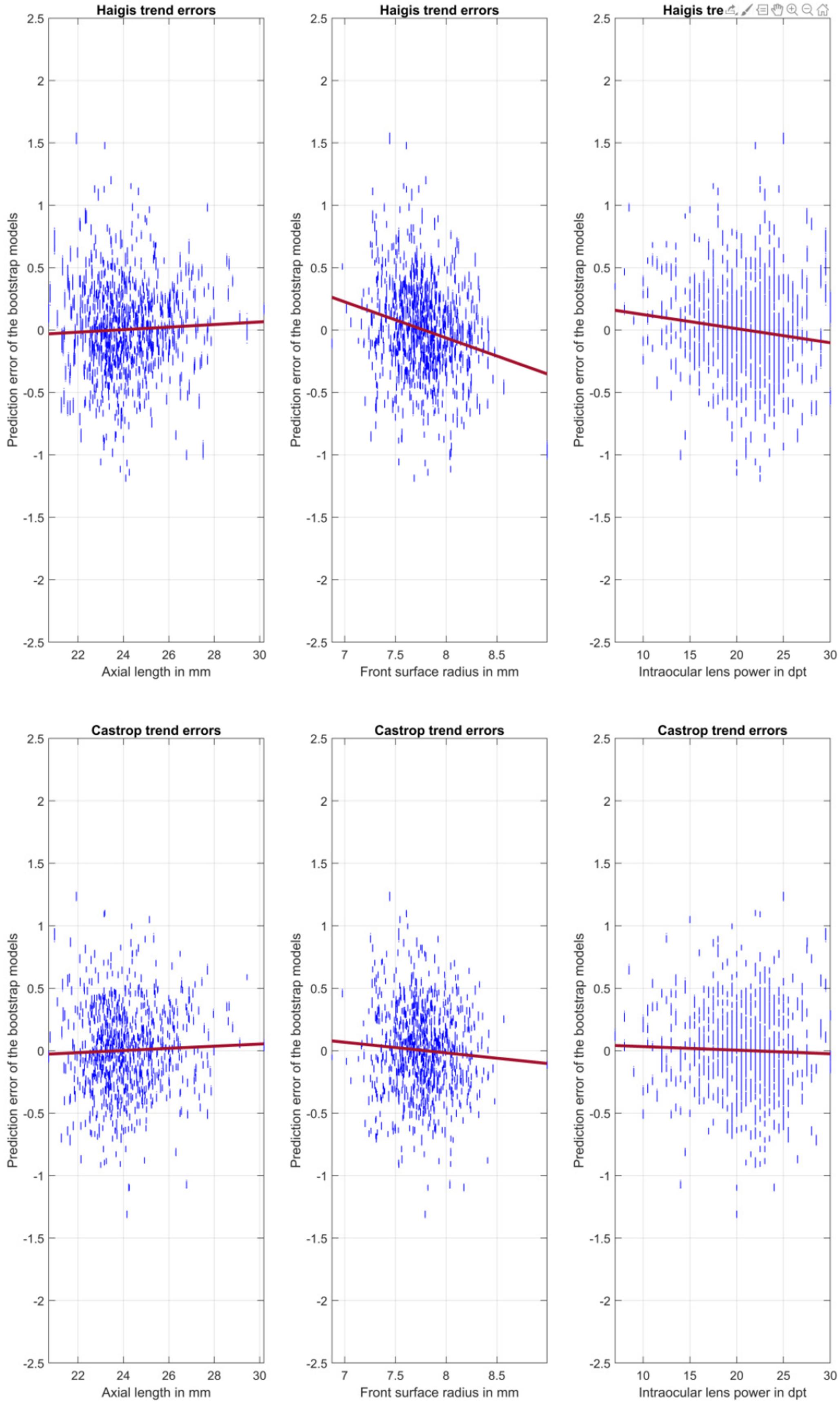

FIGURE 3 In total $N \cdot NB$ = 888 000 data points (blue) were used to determine the trend error of the 3 formulae. The results of the linear regression analysis indicate the trend error as a function of axial length (left graphs), corneal front surface radius (middle graphs) and power of the implanted intraocular lens (right graphs) for the Haigis formula (upper row), the Castrop formula (middle row) and the SRKT formula (lower row). The Haigis formula shows a slightly positive/moderate negative/slightly negative trend error for AL/Rmean/IOLP. The Castrop formula shows a slightly positive/slightly negative/no noticeable trend error for AL/Rmean/IOLP. As reference, the SRKT formula shows a moderate positive/strong positive/slightly positive trend error for AL/Rmean/IOLP.

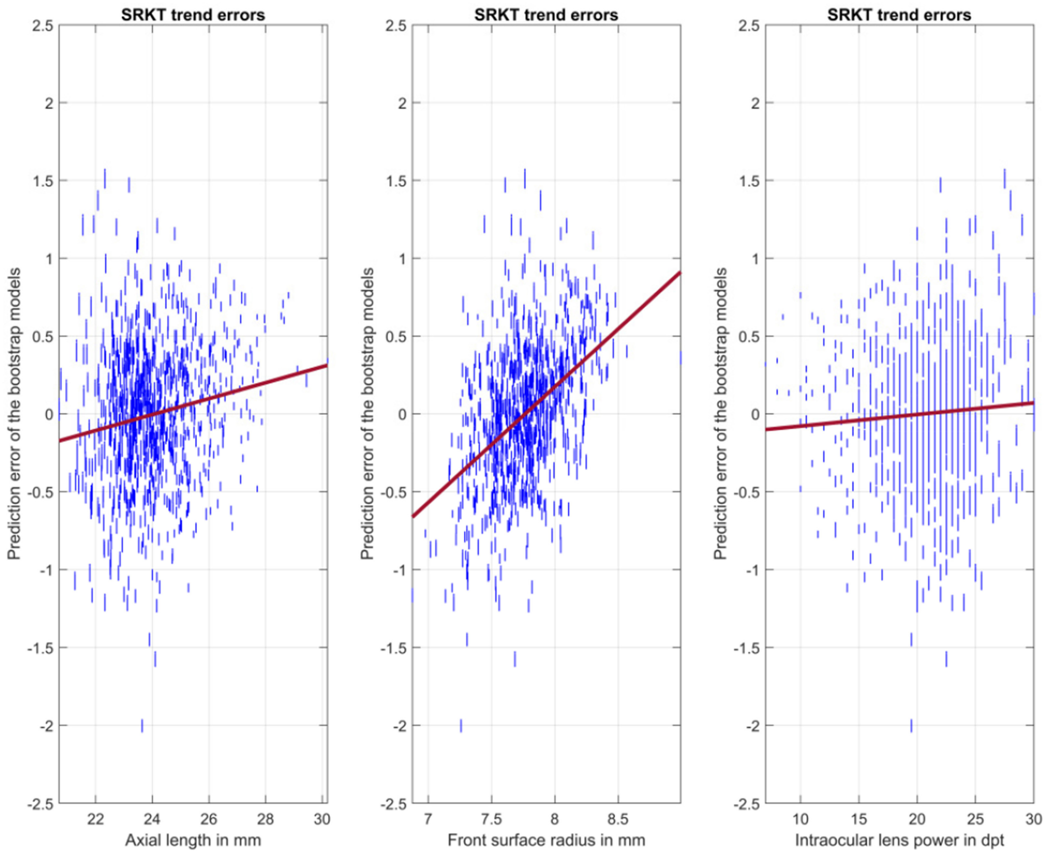

FIGURE 3 (Continued)

of squared prediction error. This formula prediction error was bootstrapped NB = 1000 times in terms of sampling with replacement and added to the formula predicted refraction derived from with the optimised formula constants (bootstrapped refraction). Then for all bootstrapped refractions a model was fitted using the same optimisation strategy as before. This means that NB = 1000 formula constant triplets (or formula constants for SRKT) are available, and the variation of these formula constants were analysed from the distribution functions as shown in Figure 1. The 90% confidence intervals for the formula constants are proper quality markers for the reliability of the formula constants and for the performance of the dataset. The narrower the confidence intervals the more consistent are the results (Worth & Cronin, 2001). Taking the Haigis formula as an example, we received a confidence interval for a0 (−0.8317 to −0.5301), which was much wider compared to the confidence interval for a1 (0.3203 to 0.3617), which was again wider compared to the confidence interval for a2 (0.1954 to 0.2100).

In a next step for all NB = 1000 sets of formula constants we back-calculated the formula prediction error from the original dataset to investigate the variation of the prediction error in terms of mean, median, mean absolute and root mean squared prediction error. For example, the standard deviation of mean, median, mean absolute and root mean squared prediction error as shown in Figure 2 give some insight how reliable the distribution of the formula prediction error would be if the experiment or study were repeated multiple times. As we used a nonlinear iterative optimisation strategy to minimise the sum of the squared prediction errors it is clear that the root mean squared prediction error (and the companion mean absolute error) in particular show a narrow distribution for all formulae, whereas the mean or median PE present a wider distribution with the NB = 1000 bootstrapped models. If our formula constants were optimised for the mean absolute PE, we would expect the mean and the median PE to show a narrower distribution for the bootstrapped data and the mean absolute and the root mean squared PE to show a wider distribution.

In a last step, we used the NB bootstrapped datasets with the N data points to extract the trend errors for those parameters, which are known to affect the predicted refraction (error) the most. From the linear regression lines in Figure 3 we can directly see that mostly the corneal front surface radius Rmean shows a major positive trend in the Haigis formula and a negative trend in the SRKT formula. That means that in situations with a flat corneal radius it is expected that on average we would end up with a hyperopic refraction with the Haigis formula and with a myopic refraction with the SRKT formula, whereas the Castrop formula is mostly unaffected by trend errors for Rmean. In addition, the SRKT formula shows a moderate positive trend error for the axial length, which means that for eyes with a large axial length (myopic eyes) the overall refraction is expected to result in hyperopia and the refraction for short eyes (hyperopic eyes) will result in myopia (Wendelstein et al., 2022). In contrast, the Haigis and the Castrop formula show only a small positive trend error for the axial length.

There are some limitations in the present study: firstly, the variation of the formula constants depends on the performance of the dataset and the metrics, which has been used for formula constant optimisation. We restricted the study to data with a postoperative visual acuity of at least 0.8 to exclude data with unreliable refractometry. We feel that minimising the sum of squared PE is a proper and highly efficient metric for constant optimisation (Langenbucher et al., 2022; Schröder et al., 2016). However, the resulting distributions may be different with other metrics and/or other target parameters. Secondly, we restricted the study to NB = 1000 bootstrapping cycles in order to keep calculations simple. With a larger number of bootstraps, the distributions for the formula constant (sets) as well as for the distribution of the bootstrapped mean, median, mean absolute and root mean squared PE after back-calculation are expected to become smoother, although this is at the cost of mathematical complexity. The entire calculation process with N = 888 data and NB = 1000 bootstraps took less than 5 seconds on a standard office PC (Intel i7 with 8 cores, 32 GB RAM). Thirdly, sampling with replacement can be seen as a good estimate, but does not fully replace a multiple repetition of the experiment/study to predict the uncertainty of the formula constants or the distribution of the PE. And last but not least, for back-calculating the PE with the formula constants from the NB bootstrap models, we used the entire dataset and did not split into in-the bag and out-of-bag data (DiCiccio & Efron, 1996; Worth & Cronin, 2001) and restrict to out-of-bag cases (which are not considered for generating the individual bootstrap model). We expect that splitting the data into in-the bag and out-of-bag cases does not noticeably change the results in our specific application.

In conclusion, this study describes the application of bootstrap strategies to the prediction of formula constant uncertainties and the variation of the formula prediction error for intraocular lens power calculation with 3 theoretical-optical formulae. A clinical dataset with N = 888 eyes was used to show how to extract the uncertainty of the a0/a1/a2 constant triplet for the Haigis formula, the C/H/R constant triplet for the Castrop formula, and the A constant for the SRKT formula as reference, and the respective metrics (mean, median, mean absolute and root mean squared value) of the formula prediction error in combination with a nonlinear iterative constant optimisation technique.

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